

GenCore version 4.5  
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OM protein - protein search, using sw model

Run on: September 27, 2001, 16:40:52 ; Search time 16.74 seconds

(without alignments)  
650.731 Million cell updates/sec

Title: US-09-483-543a-8

Perfect score: 1693  
Sequence: 1 KRGCAGNEDSEERSSMYGR.....QQNPDEDFSGCGXGLEVLFLQ 318

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 93435 seqs, 34255486 residues

Total number of hits satisfying chosen parameters: 93435

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database : SwissProt\_39.\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

## SUMMARIES

Result No.	Score	Query Match	Length	ID	Description
1	1612	95.2	304	1 CRK_MOUSE	064010 mus musculu
2	1605	94.8	304	1 CRK_RAT	063768 rattus norv
3	1588	93.8	304	1 CRK_HUMAN	P46108 homo sapien
4	1379.5	81.5	305	1 CRK_CHICK	004929 gallus gall
5	1315	77.7	296	1 CRK_XENLA	P87378 xenopus lae
6	917.5	54.2	303	1 CRKL_HUMAN	P46109 homo sapien
7	911.5	53.8	303	1 CRKL_MOUSE	P47941 mus musculu
8	818.5	48.3	440	1 GAGC_AYISC	P05433 avian sarco
9	642.5	38.0	271	1 CRK_DROME	Q9XJN0 drosophila
10	257	15.2	217	1 GRAP_HUMAN	Q13568 homo sapien
11	236	13.9	211	1 DRK_DROME	Q08012 drosophila
12	224	13.2	217	1 GRB2_HUMAN	P29334 homo sapien
13	224	13.2	217	1 GRB2_MOUSE	060631 mus musculu
14	218	12.9	217	1 GRB2_CHICK	007883 gallus gall
15	214	12.6	217	1 GRB2_XENLA	P87379 xenopus lae
16	202	11.9	228	1 SEM5_CAEEL	P29335 caenorhabdi
17	184	10.9	1291	1 PIG1_BOVIN	P08457 bos taurus
18	178	10.5	1290	1 PIG1_HUMAN	P19174 homo sapien
19	177	10.5	1290	1 PIG1_RAT	P10666 rattus norv
20	174.5	10.3	322	1 GRP2_MOUSE	089100 m grib2-reia
21	174	10.3	845	1 VAV_HUMAN	P15498 homo sapien
22	173	10.2	843	1 VAV_MOUSE	P54100 rattus norv
23	167	9.9	845	1 VAV_MOUSE	P27870 mus musculu
24	159.5	9.4	847	1 VAV3_HUMAN	Q9UK44 homo sapien
25	158.5	9.4	330	1 GRP2_HUMAN	Q15811 h grib2-reia
26	157	9.3	520	1 ITSN_HUMAN	Q15811 homo sapien
27	155.5	9.2	847	1 VAV3_MOUSE	Q91068 mus musculu
28	154.5	9.1	878	1 VAV2_HUMAN	P52735 homo sapien
29	151	8.9	1168	1 MISC_ACRCA	P10569 acanthamoeb
30	150	8.9	960	1 DTGL_DROME	P31007 drosophila
31	148.5	8.8	868	1 VAV2_MOUSE	Q60992 mus musculu
32	148.5	8.8	1113	1 MYSD_DICDI	P41010 dictyostell
33	147	8.7	1044	1 GRPA_BOVIN	P09851 bos taurus

34	146.5	8.7	1038	1 GRPA_RAT	P50904 rattus norv
35	146	8.6	946	1 RHGA_HUMAN	P98171 homo sapien
36	144.5	8.5	1047	1 GRPA_HUMAN	P20936 homo sapien
37	142	8.4	450	1 CSK_CHICK	P41239 gallus gall
38	139	8.2	359	1 YKA7_CAEEL	P34258 caenorhabdi
39	139	8.2	1196	1 ABU1_CAEEL	P03949 caenorhabdi
40	138.5	8.2	505	1 SRK1_SPOLA	P42686 spomgilla 1
41	138.5	8.2	1265	1 PIG2_RAT	P24135 rattus norv
42	138	8.2	583	1 SHC_HUMAN	P29353 homo sapien
43	137.5	8.1	578	1 SHC_MOUSE	P98083 mus musculu
44	136	8.0	450	1 CSK_HUMAN	P41240 homo sapien
45	134	7.9	450	1 CSK_MOUSE	P41241 mus musculu

## ALIGNMENTS

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RESULT 1
CRK_MOUSE          STANDARD:      PRT;      304 AA.
ID CRK_MOUSE
AC 064010;
DT 01-NOV-1997 (Rel. 35, Created)
DT 01-NOV-1997 (Rel. 35, Last sequence update)
DT 15-JUL-1999 (Rel. 38, Last annotation update)
DE PROTO-ONCOGENE C-CRK (P38) (ADAPTER MOLECULE CRK).
OS CRK OR CRKO.
OC Mus musculus (Mouse).
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Mus.
OX NCBI_Taxid=10090;
RN [1]
RP SEQUENCE FROM N.A.
RC TISSUE=Liver;
RX MEDLINE=94239744; PubMed=8183562;
RA Ogawa S., Toyoshima H., Kozutsumi H., Hagiwara K., Sakai R.,
RA Tanaka T., Hirano N., Mano H., Yazaki Y., Hirai H.;
RT "The C-terminal SH3 domain of the mouse c-crk protein negatively
RT regulates tyrosine-phosphorylation of Crk associated pl30 in rat 3Y1
RT cells."
RL Oncogene 9:1669-1678(1994).
RN [2]
RP X-RAY CRYSTALLOGRAPHY (1.5 ANGSTROMS) OF 134-190.
RX MEDLINE=95253821; PubMed=7735837;
RA Wu X., Knudsen B., Feller S.M., Zheng J., Sali A., Cowburn D.,
RA Hanafusa H., Kuriyan J.;
RT "Structural basis for the specific interaction of lysine-containing
RT proline-rich peptides with the N-terminal SH3 domain of c-Crk."
RL Structure 3:215-226(1995).
RN [3]
RP X-RAY CRYSTALLOGRAPHY (2.5 ANGSTROMS) OF 133-191.
RX MEDLINE=99069628; PubMed=9851931;
RA Nguyen J.T., Turk C.W., Cohen F.E., Zuckermann R.N., Lim W.A.;
RT "Exploiting the basis of proline recognition by SH3 and WW domains:
RT design of N-substituted inhibitors."
RL Science 282:2088-2092(1998).
CC -I- FUNCTION: THE CRK-I AND CRK-II FORMS DIFFER IN THEIR BIOLOGICAL
CC ACTIVITIES. CRK-II HAS LESS TRANSFORMING ACTIVITY THAN CRK-I. BOTH
CC CRK-I AND CRK-II BIND TO MANY OF TYROSINE-PHOSPHORYLATED PROTEINS
CC THAT BIND TO GRB2.
CC -I- ALTERNATIVE PRODUCTS: 2 ISOFORMS: CRK-I AND CRK-II (SHOWN HERE);
CC ARE PRODUCED BY ALTERNATIVE SPLICING. THE CRK-I FORM LACKS THE
CC LAST 100 RESIDUES.
CC -I- TISSUE SPECIFICITY: UBQUITOUS.
CC -I- DOMAIN: THE C-TERMINAL SH3 DOMAIN FUNCTION AS A NEGATIVE MODULATOR
CC FOR TRANSFORMATION AND THE N-TERMINAL SH3 DOMAIN APPEARS TO
CC FUNCTION AS A POSITIVE REGULATOR FOR TRANSFORMATION (BY
CC SIMILARITY).
CC -I- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -I- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
CC -----
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DR EMBL: S72408; AAB30755.1; -

DR PDB: 1CKA; 08-MAY-95.

DR PDB: 1CKB; 08-MAY-95.

DR PDB: 1B07; 06-JAN-99.

DR MGI: 88508; Crko.

DR InterPro: IPR000980; -

DR InterPro: IPR001452; -

DR Pfam: PF00017; SH2; 1.

DR Pfam: PF00018; SH3; 1.

DR PRINTS: PR00401; SH2DOMAIN.

DR PRINTS: PR00452; SH3DOMAIN.

DR PROSITE: PS50001; SH2; 1.

DR PROSITE: PS50002; SH3; 1.

DR PROSITE: PS50003; SH3; 1.

KM Phosphorylation; SH2 domain; SH3 domain; Alternative splicing;

KM Phosphorylation; 3D-structure.

FT DOMAIN 13 118 SH2.

FT DOMAIN 132 192 SH3.

FT DOMAIN 256 296 SH3.

FT VASPLC 205 304 MISSING (IN ISOFORM CRK-I).

SQ SEQUENCE 304 AA; 33814 MW; 5491896FC7A89065 CRC64;

Query Match 95.2%; Score 1612; DB 1; Length 304;

Best Local Similarity 100.0%; Pred. No. 4.2e-109; Mismatches 0; Indels 0; Gaps 0;

Matches 303; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 5 AGNFDSEERSWYMGRLSRQEAVALLOGRHGVFLVRDSTSPGDVYLSVSENSRVSHYI 64

DB 2 AGNFDSEERSWYMGRLSRQEAVALLOGRHGVFLVRDSTSPGDVYLSVSENSRVSHYI 61

QY 65 INSSGPRPPVPPSPAPPGVSPSRIRIGDQFDSLPALLEFYKIHLYDTTLLIEPVARS 124

DB 62 INSSGPRPPVPPSPAPPGVSPSRIRIGDQFDSLPALLEFYKIHLYDTTLLIEPVARS 121

QY 125 ROGSGLVLRQEALEYRALFDENGDEEDLPFKKGDILIRDKREEDQWMADESGKRG 184

DB 122 ROGSGLVLRQEALEYRALFDENGDEEDLPFKKGDILIRDKREEDQWMADESGKRG 181

QY 185 IPVPEYKRRPASASVSALLIGNQESHHPOLGPGPEPGYAPSVNTPLPNLQNGPIYAR 244

DB 182 IPVPEYKRRPASASVSALLIGNQESHHPOLGPGPEPGYAPSVNTPLPNLQNGPIYAR 241

QY 245 VIOKRVPAVYKLTALALEVGLVYKTKINVSQWEGECNGKRGHPPTHVRLDQONPDE 304

DB 242 VIOKRVPAVYKLTALALEVGLVYKTKINVSQWEGECNGKRGHPPTHVRLDQONPDE 301

QY 305 DFS 307

DB 302 DFS 304

RESULT 2

CRK\_RAT STANDARD; PRT; 304 AA.

ID CRK\_RAT

AC 063768;

DT 01-NOV-1997 (Rel. 35, Created)

DT 01-NOV-1997 (Rel. 35, Last sequence update)

DT 01-OCT-2000 (Rel. 40, Last annotation update)

DE PROTO-ONCOGENE C-CRK (P38) (ADAPTER MOLECULE CRK).

GN CRK.

OS Rattus norvegicus (Rat).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.

OX NCBI\_TaxID=10116;

RN [1]

RP SEQUENCE FROM N.A.

RC TISSUE=Kidney;

RX MEDLINE=97057214; PubMed=8901553;

RA Kizaka-Kondoh S., Matsuda M., Okayama H.;

RT "CrkII signals from epidermal growth factor receptor to Ras";

RL Proc. Natl. Acad. Sci. U.S.A. 93:12177-12182(1996).

CC -I- FUNCTION: THE CRK-I AND CRK-II FORMS DIFFER IN THEIR BIOLOGICAL

CC ACTIVITIES. CRK-II HAS LESS TRANSFORMING ACTIVITY THAN CRK-I. BOTH

CC CRK-I AND CRK-II BIND TO MANY OF TYROSINE-PHOSPHORYLATED PROTEINS

CC THAT BIND TO GRB2

CC -I- ALTERNATIVE PRODUCTS: 2 ISOFORMS; CRK-I AND CRK-II (SHOWN HERE);

CC ARE PRODUCED BY ALTERNATIVE SPLICING. THE CRK-I FORM LACKS THE

CC LAST 100 RESIDUES.

CC -I- TISSUE SPECIFICITY: CRK-II IS EXPRESSED IN ALL TISSUES AND CELLS

CC WHEREAS CRK-I IS EXPRESSED AT LOWER LEVEL AND IN LIMITED CELL-

CC TYPES.

CC -I- DOMAIN: THE C-TERMINAL SH3 DOMAIN FUNCTION AS A NEGATIVE MODULATOR

CC FOR TRANSFORMATION AND THE N-TERMINAL SH3 DOMAIN APPEARS TO

CC FUNCTION AS A POSITIVE REGULATOR FOR TRANSFORMATION (BY

CC SIMILARITY).

CC -I- SIMILARITY: CONTAINS 1 SH2 DOMAIN.

CC -I- SIMILARITY: CONTAINS 2 SH3 DOMAINS.

CC -----

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CC -----

DR EMBL: D44481; BAA07924.1; -

DR HSSP: Q64010; 1CKB.

DR InterPro: IPR000980; -

DR InterPro: IPR001452; -

DR Pfam: PF00017; SH2; 1.

DR Pfam: PF00018; SH3; 1.

DR PRINTS: PR00401; SH2DOMAIN.

DR PRINTS: PR00452; SH3DOMAIN.

DR PROSITE: PS50001; SH2; 1.

DR PROSITE: PS50002; SH3; 1.

KM Proto-oncogene; SH2 domain; SH3 domain; Alternative splicing;

KM Phosphorylation.

FT DOMAIN 13 118 SH2.

FT DOMAIN 132 192 SH3.

FT DOMAIN 256 296 SH3.

FT VASPLC 205 304 MISSING (IN ISOFORM CRK-I).

FT VARIANT 244 244 Q -> R (NRK-23 INACTIVE MUTANT).

FT VARIANT 253 253 K -> E (NRK-23 INACTIVE MUTANT).

SQ SEQUENCE 304 AA; 33844 MW; 4CFBF85BE72E265 CRC64;

Query Match 94.8%; Score 1605; DB 1; Length 304;

Best Local Similarity 99.3%; Pred. No. 1.3e-108; Mismatches 2; Indels 0; Gaps 0;

Matches 301; Conservative 2; Mismatches 0; Indels 0; Gaps 0;

QY 5 AGNFDSEERSWYMGRLSRQEAVALLOGRHGVFLVRDSTSPGDVYLSVSENSRVSHYI 64

DB 2 AGNFDSEERSWYMGRLSRQEAVALLOGRHGVFLVRDSTSPGDVYLSVSENSRVSHYI 61

QY 65 INSSGPRPPVPPSPAPPGVSPSRIRIGDQFDSLPALLEFYKIHLYDTTLLIEPVARS 124

DB 62 INSSGPRPPVPPSPAPPGVSPSRIRIGDQFDSLPALLEFYKIHLYDTTLLIEPVARS 121

QY 125 ROGSGLVLRQEALEYRALFDENGDEEDLPFKKGDILIRDKREEDQWMADESGKRG 184

DB 122 ROGSGLVLRQEALEYRALFDENGDEEDLPFKKGDILIRDKREEDQWMADESGKRG 181

QY 185 IPVPEYKRRPASASVSALLIGNQESHHPOLGPGPEPGYAPSVNTPLPNLQNGPIYAR 244

DB 182 IPVPEYKRRPASASVSALLIGNQESHHPOLGPGPEPGYAPSVNTPLPNLQNGPIYAR 241

QY 245 VIOKRVPAVYKLTALALEVGLVYKTKINVSQWEGECNGKRGHPPTHVRLDQONPDE 304

DB 242 VIOKRVPAVYKLTALALEVGLVYKTKINVSQWEGECNGKRGHPPTHVRLDQONPDE 301

QY 305 DFS 307  
111  
Db 302 DFS 304

RESULT 3  
CRK\_HUMAN STANDARD: PRT; 304 AA.

AC P46108;  
DT 01-NOV-1995 (Rel. 32, Created)  
DT 01-NOV-1995 (Rel. 32, Last sequence update)  
DT 01-OCT-2000 (Rel. 40, Last annotation update)  
DE PROTO-ONCOGENE C-CRK (P38) (ADAPTER MOLECULE CRK).  
GN CRK.  
OS Homo sapiens (Human).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Mammalia; Eutheria; Primates; Catarrhini; Homidae; Homo.  
OX NCBI\_TaxId=9606;  
RN [1]  
RP SEQUENCE FROM N.A.  
RC TISSUE=Embryonic Lung, and Placenta;  
RX MEDLINE=92334347; PubMed=1630456;  
RA Matsuda M., Tanaka S., Nagata S., Kojima A., Kurata T., Shibuya M.;  
RT "Two species of human CRK cDNA encode proteins with distinct  
RT biological activities."  
RL Mol. Cell. Biol. 12:3482-3489(1992).  
RN [2]  
RP SEQUENCE FROM N.A.  
RX MEDLINE=93390962; PubMed=8378094;  
RA Fioretos T., Heisterkamp N., Groffen J., Benjes S., Morris C.;  
RT "CRK proto-oncogene maps to human chromosome band 17p13."  
RL Oncogene 8:2853-2855(1993).  
CC -1- FUNCTION: THE CRK-I AND CRK-II FORMS DIFFER IN THEIR BIOLOGICAL  
CC ACTIVITIES. CRK-II HAS LESS TRANSFORMING ACTIVITY THAN CRK-I. BOTH  
CC CRK-I AND CRK-II BIND TO MANY OF TYROSINE-PHOSPHORYLATED PROTEINS  
CC THAT BIND TO GRB2.  
CC -1- ALTERNATIVE PRODUCTS: 2 ISOFORMS: CRK-I AND CRK-II (SHOWN HERE);  
CC ARE PRODUCED BY ALTERNATIVE SPLICING. THE CRK-I FORM LACKS THE  
CC LAST 100 RESIDUES.  
CC -1- DOMAIN: THE C-TERMINAL SH3 DOMAIN FUNCTION AS A NEGATIVE MODULATOR  
CC FOR TRANSFORMATION AND THE N-TERMINAL SH3 DOMAIN APPEARS TO  
CC FUNCTION AS A POSITIVE REGULATOR FOR TRANSFORMATION.  
CC -1- PTM: PHOSPHORYLATION OF CRK-II (40 KDA) GIVES RISE TO A 42 KDA  
CC FORM.  
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.  
CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.  
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CC EMBL: D10656; BAA01505.1; -;  
DR EMBL: S65701; AAB38213.1; -;  
DR HSSP: Q64010; ICKB.  
DR SWISS-2DPAGE; P46108; HUMAN.  
DR MIM; 164762; -;  
DR InterPro; IPR000980; -;  
DR InterPro; IPR001452; -;  
DR Pfam; PF00017; SH2; 1.  
DR Pfam; PF00018; SH3; 1.  
DR PRINTS; PR00401; SH2DOMAIN.  
DR PRINTS; PR00452; SH3DOMAIN.  
DR PROSITE; PS50001; SH2; 1.  
DR PROSITE; PS50002; SH3; 1.  
DR Proto-oncogene; SH2 domain; SH3 domain; Alternative splicing;  
KW Phosphorylation.  
FT DOMAIN 13 118 SH2.  
FT DOMAIN 132 192 SH3.  
FT DOMAIN 256 296 SH3.

FT VARSPIC 205 304 MISSING (IN ISOFORM CRK-I).  
SQ SEQUENCE 304 AA; 33872 MW; D74A83ED1FFC0EBC CRC64;  
Query Match 93.8%; Score 1588; DB 1; Length 304;  
Best Local Similarity 98.7%; Pred. No. 2, 2e-107;  
Matches 299; Conservative 1; Mismatches 3; Indels 0; Gaps 0;

QY 5 AGNDESESRSSWYWGRLSRQEAVALLOGQRHGVFLVBDSTSPGDYVLSVENSRYSHYI 64  
DB 2 AGNFSESRSSWYWGRLSRQEAVALLOGQRHGVFLVBDSTSPGDYVLSVENSRYSHYI 61  
QY 65 INSSGPRPPVPPSPAPGVPSPRLRGDOFDSLALLEFYIHIHLDITTLIEPARS 124  
DB 62 INSSGPRPPVPPSPAPGVPSPRLRGDOFDSLALLEFYIHIHLDITTLIEPARS 121  
QY 125 ROGSGVILROEAEFVRLPFGNGDEEDLPEFKGDLIRTDKPEEOMWNAESEGKGM 184  
DB 122 ROGSGVILROEAEFVRLPFGNGDEEDLPEFKGDLIRTDKPEEOMWNAESEGKGM 181  
QY 185 IPVPYVEKYPASASVSALLIGNEGSHPOPLGGPEPGPYAOPSVNTPLDNLQNGPIYAR 244  
DB 182 IPVPYVEKYPASASVSALLIGNEGSHPOPLGGPEPGPYAOPSVNTPLDNLQNGPIYAR 241  
QY 245 VIQKRVPAAYDKTALALEVGLVYVTKINVSQWEGECNGKRGHPPTTHVRLDQNPDE 304  
DB 242 VIQKRVPAAYDKTALALEVGLVYVTKINVSQWEGECNGKRGHPPTTHVRLDQNPDE 301

QY 305 DFS 307  
111  
Db 302 DFS 304

RESULT 4  
CRK\_CHICK STANDARD: PRT; 305 AA.

AC Q04929;  
DT 01-NOV-1995 (Rel. 32, Created)  
DT 01-NOV-1995 (Rel. 32, Last sequence update)  
DT 01-NOV-1995 (Rel. 32, Last annotation update)  
DE PROTO-ONCOGENE C-CRK (P38).  
GN CRK.  
OS Gallus gallus (Chicken).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;  
OC Gallus.  
OX NCBI\_TaxId=9031;  
RN [1]  
RP SEQUENCE FROM N.A.  
RX MEDLINE=93041379; PubMed=1329926;  
RA Reichman C.T., Mayer B.J., Khawer S., Hanafusa H.;  
RT "The product of the cellular crk gene consists primarily of SH2 and  
RT SH3 regions."  
RL Cell Growth Differ. 3:451-460(1992).  
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.  
CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.  
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CC EMBL: L08168; AAA49001.1; -;  
DR HSSP: Q64010; ICKB.  
DR InterPro; IPR000980; -;  
DR InterPro; IPR001452; -;  
DR Pfam; PF00017; SH2; 1.  
DR Pfam; PF00018; SH3; 1.  
DR PRINTS; PR00401; SH2DOMAIN.  
DR PRINTS; PR00452; SH3DOMAIN.

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DR      InterPro:IPR001452; -
DR      Pfam; PF00017; SH2; 1.
DR      Pfam; PF00018; SH3; 1.
DR      PRINTS; PR00401; SH2DOMAIN.
DR      PRINTS; PR00452; SH3DOMAIN.
DR      PROSITE; PS50001; SH2; 1.
DR      PROSITE; PS50002; SH3; 1.
KW      SH2 domain; SH3 domain.
FT      DOMAIN      13      112      SH2.
FT      DOMAIN      125      185      SH3.
FT      DOMAIN      249      289      SH3.
SQ      SEQUENCE      296 AA; 33409 MM; 544T11FA41F75A66 CRC64;

Query Match      77.7%; Score 1315; DB 1; Length 296;
Best Local Similarity 82.88; Pred. No. 9e-88;
Matches 251; Conservative 21; Mismatches 23; Indels 8; Gaps 3;

QY      5 AGNPFDEERSWYMGRLRROEAVALLQQRGQVFLVDRDSTSPGQYVLVSSENSRSHYI 64
DB      2 AGNPFDEERSWYMGRLRROEAVALLQQRGQVFLVDRDSTSPGQYVLVSSENSRSHYI 61
QY      65 INSSGPRPPVPPSPAPPPGVSPSLRIGDGEFDSLPALEPKYKHYLDITTLLEPVARS 124
DB      62 INS-----VTNNRQSSTAGWQSFRRIGDGEFDSLPLLEFYKHYLDITTLLEPVARS 115
QY      125 RQSGCVILRQEAEEVRLAPFNGNDEEDLPFKKDIIRIDKPEEQWNAEDSGRGM 184
DB      116 KQ-SCVIRQEEVEIRLALPFIQNDDEDLPFKKDIIRIEKPEEQWNAEDSGRGM 174
QY      185 IPVPEYKRYRPAASVSALIGNQEGSHPOPLGEGPQPYAQPVSNTPLPILQNSPIYAR 244
DB      175 IPVPEYKRYRPPSPGSAALIGQNGENSHPOPLGEGPQPYAQPVSNTPLPILQNSPIAR 234
QY      245 VIQKRVPAVYKKTALALEVGLVYKTKINVSQMGQEGCGKRGHPFHVLLDQNDPE 304
DB      235 VIQKRVPAVYKKTALALEVGLVLTAKYTKINVSQMGQEGCGKRGHPFHVRL-LQNDPE 293
QY      305 DFS 307
DB      294 DFS 296

RESULT      6
CRKL_HUMAN CRKL_HUMAN STANDARD; PRT; 303 AA.
AC      P46109;
DT      01-NOV-1995 (Rel. 32, Created)
DT      01-NOV-1995 (Rel. 32, Last sequence update)
DT      01-OCT-2000 (Rel. 40, Last annotation update)
DE      CRK-LIKE PROTEIN.
GN      CRKL.
OS      Homo sapiens (Human).
OC      Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC      Mammalia; Eutheria; Primates; Catarrhini; Homnidae; Homo.
OX      NCBI_TaxId=9606;
RN      [1]
RP      SEQUENCE FROM N.A.
RC      TISSUE=Spleen;
RX      MEDLINE=93368949; Pubmed=8361759;
RA      ten Hoeve J., Morris C., Heisterkamp N., Groffen J.;
RT      Isolation and chromosomal localization of CRKL, a human crk-like
RT      gene.";
RL      Oncogene 8:2469-2474(1993).
CC      -1- FUNCTION: MAY MEDIATE THE TRANSDUCTION OF INTRACELLULAR SIGNALS.
CC      -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC      -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
CC      -----
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DR EMBL: AF112976; AAD28428.1; -.
DR HSP: Q64010; ICKA.
DR FlyBase: FBgn0024811; Ctk.
DR InterPro: IPR000980; -.
DR InterPro: IPR001452; -.
DR Pfam: PF00017; SH2; 1.
DR Pfam: PF00018; SH3; 1.
DR PRINTS: PR00401; SH2DOMAIN.
DR PRINTS: PR00452; SH3DOMAIN.
DR PROSITE: PS50001; SH2; 1.
DR PROSITE: PS50002; SH3; 1.
DR SH2 domain; SH3 domain; Developmental protein.
KW DOMAIN 12 114 SH2.
FT DOMAIN 117 165 SH3.
FT DOMAIN 220 259 SH3.
SQ SEQUENCE 271 AA; 31205 MW; D1B4FE43150932DC CRC64;

Query Match 38.0%; Score 642.5; DB 1; Length 271;
Best Local Similarity 43.8%; Pred. No. 1.7e-39;
Matches 133; Conservative 42; Mismatches 68; Indels 61; Gaps 6;

QY 8 FDEEERSSWTWGLSRQEAVALLOQR-HGVLYRDSSTSPGCVLVSYSENSKVHYIIN 66
   ||:||||:||||:|:| |||||:|:| |||||:|:| |||||:|:| |||||:|:|
DB 4 FVYSDRNSWYFGFMSQDATEVLMNERGVFLVSDNSIAGDYLCVREDTKVSNYIIN 63
QY 67 SSGPRPPVPPSPAQPPGVSPSLRIGDGFSLPALLEFYKIHVDTTLLPEVARSRO 126
   :|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|
DB 64 KVOQOQOIV-----YRIGDOSFDLPRKILFFYTHLYDTTPPKRPACR--- 106
QY 127 GSGVILLROEAEYRVALFDENGDEEDLPKKGDLIRIDKPEEOMWNAEDSGKRGMT 186
   -|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|
DB 107 -----RVEKVIKGFDEVGSDODDLPFOGRGEVLTIVAKDEDMWTFARNSSGKIGQIP 157
QY 187 VEVYERY-----RPASVSAALIGNQBSHQPLGGRPPGPAQSVNTPLP 234
   |||:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|
DB 158 VPTQOIDDYMDDAIDKNEPSISGSNVEFSTLK-----RDLNRKLI- 200
QY 235 NLONGPIYAVIOKRVNAYDKTALALEVGLVKTAKINVGOMEGECNGKRGHPFTHY 294
   | ||||| | ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
DB 201 ----PAYAVKQSRVPMATKALKEIGDIIKVTKTNTNGWBEELNKGNGHFFTHV 255
QY 295 RLID 298
   :|
DB 256 EFVD 259

RESULT 10
GRAP_HUMAN STANDARD; PRT; 217 AA.
ID GRAP_HUMAN
AC 013588;
DT 15-DEC-1998 (Rel. 37, Created)
DT 15-DEC-1998 (Rel. 37, Last sequence update)
DT 01-OCT-2000 (Rel. 40, Last annotation update)
DE GRB2-RELATED ADAPTOR PROTEIN.
GN GRAP.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Homiidae; Homo.
NCBI_TaxID=9606;
RN [1]
RP SEQUENCE FROM N.A.
RX MEDLINE=96218119; PubMed=8647802;
RA Peng G.-S., Ouyang Y.-B., Hu D.-P., Shi Z.-Q., Gentz R., Ni J.;
RT "Grp is a novel SH3-SH2-SH3 adaptor protein that couples tyrosine
RT kinases to the Ras pathway.";
RL J. Biol. Chem. 271:12129-12132(1996).
CC -!- FUNCTION: COUPLE SIGNALS FROM RECEPTOR AND CYTOPLASMIC TYROSINE
CC KINASES TO THE RAS SIGNALING PATHWAY.
CC -!- SUBUNIT: ASSOCIATES THROUGH ITS SH2 DOMAIN WITH LIGAND-ACTIVATED
CC RECEPTORS FOR STEM CELL FACTOR (KIT) AND ERYTHROPOIETIN (EPOR).
CC ALSO FORMS A STABLE COMPLEX WITH THE BCR-ABL ONCOPROTEIN. GRAP IS
CC ASSOCIATED WITH THE RAS GUANINE NUCLEOTIDE EXCHANGE FACTOR SOS1,

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CC CC PRIMARILY THROUGH ITS N-TERMINAL SH3 DOMAIN.
CC -!- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -!- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
CC -!- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.
CC -----
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CC or send an email to license@isb-sib.ch).
CC -----
DR EMBL: U52518; AAC50541.1; -.
DR MIM: 604330; -.
DR InterPro: IPR000980; -.
DR InterPro: IPR001452; -.
DR Pfam: PF00017; SH2; 1.
DR Pfam: PF00018; SH3; 2.
DR PRINTS: PR00452; SH3DOMAIN.
DR PROSITE: PS50001; SH2; 1.
DR PROSITE: PS50002; SH3; 2.
KW SH2 domain; SH3 domain.
FT DOMAIN 1 58 SH3.
FT DOMAIN 60 152 SH2.
FT DOMAIN 156 215 SH3.
SQ SEQUENCE 217 AA; 25336 MW; 09FEC2F3BAC0FAF8 CRC64;

Query Match 15.2%; Score 257; DB 1; Length 217;
Best Local Similarity 31.4%; Pred. No. 6.4e-12;
Matches 64; Conservative 40; Mismatches 54; Indels 46; Gaps 9;

QY 2 RGCAG----NFDSEERSWYMGRLSRQEAVALLOQRH-GVFLVDSSTSPGCVLVSYSE 56
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DB 42 RVEGEFIPKNTIRVKNPHRYSGRISQLAEELMRNLGAFILRESSSGEESVSNY 101
QY 57 NSRVSHYII--NSSGPRPPVPPSPAQPPGVSPSLRIGDGFSLPALLEFYKIHVDT 114
   :|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|
DB 102 GQOVHFVKVLRASG-----KYFLMEEEKFNLSNLTVDYFR-----T 137
QY 115 TTLIEPVARSRGSGVILLROE-----AEYRALFDPNGDEEDLPFKGDLIRIDK 167
   ||:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|
DB 138 TT----IARKRQ--IFLRDEEPLKSPACFAQDFSAODPSQLSFRGDIIEVLER 190
QY 168 PEEOMWNAEDSEKRGMTVPYVE 191
   |:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|:|
DB 191 PDPHMKGR-SCGRVGFPPRSTVQ 213

RESULT 11
DRK_DROME STANDARD; PRT; 211 AA.
ID DRK_DROME
AC 008012; Q9Y605;
DT 01-FEB-1995 (Rel. 31, Created)
DT 01-FEB-1995 (Rel. 31, Last sequence update)
DT 01-OCT-2000 (Rel. 40, Last annotation update)
DE PROTEIN K(Sev)2B (SH2-SH3 ADAPTOR PROTEIN DRK).
GN DRK OR E(Sev)2B OR CG6033.
OS Drosophila melanogaster (fruit fly).
OC Eukaryota; Metazoa; Arthropoda; Tracheata; Hexapoda; Insecta;
OC Pterygota; Neoptera; Endopterygota; Diptera; Brachycera; Muscomorpha;
OC Ephydroidea; Drosophilidae; Drosophila.
NCBI_TaxID=7227;
RN [1]
RP SEQUENCE FROM N.A.
RC TTSUB=Eye;
RX MEDLINE=93214989; PubMed=8462097;
RA Simon M.A., Dodson G.S., Rubin G.M.;
RT "An SH3-SH2-SH3 protein is required for p21Ras1 activation and binds
RT to sevenless and Sos proteins in vitro.";
RL Cell 73:169-177(1993).
RN [2]

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RT libraries.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 89:9015-9019(1992).  
 RL [3]  
 RP SEQUENCE FROM N.A., AND ALTERNATIVE SPLICING.  
 RC SPECIES-Rat; STRAIN-Wistar; TISSUE-Brain;  
 RX MEDLINE-95293967; PubMed-775428;  
 RA Watanabe K., Fukuchi T., Hosoya H., Shirasawa T., Matsuo K.,  
 RA Miki H., Takenawa T.;  
 RT "Splicing isoforms of rat Ash/Grb2. Isolation and characterization of  
 RT the cDNA and genomic DNA clones and implications for the  
 RT physiological roles of the isoforms.";  
 RL J. Biol. Chem. 270:13733-13739(1995).  
 RN [4]  
 RP SEQUENCE FROM N.A. (ISOFORM GRB2-3).  
 RC SPECIES-Human; TISSUE-Placenta;  
 RX MEDLINE-94233382; PubMed-8178156;  
 RA Path I., Schweighoffer F., Rey I., Multon M.C., Boiziau J.,  
 RA Duchesne M., Tocque B.;  
 RT "Cloning of a Grb2 isoform with apoptotic properties.";  
 RL Science 264:971-974(1994).  
 RN [5]  
 RP SEQUENCE FROM N.A.  
 RC SPECIES-Human; TISSUE-Epidermis;  
 RX MEDLINE-99162407; PubMed-10051406;  
 RA Boelmann H., Gehrisch S., Jaross W.;  
 RT "The gene structure of the human growth factor bound protein GRB2.";  
 RL Genomics 56:203-207(1999).  
 RN [6]  
 RP ASSOCIATION WITH IRS-1.  
 RX MEDLINE-9326558; PubMed-8388384;  
 RA Tobe K., Matuoka K., Tamemoto H., Ueki K., Kaburagi Y., Asai S.,  
 RA Noguchi T., Matsuda M., Tanaka S., Hattori S., Fukui Y., Akanuma Y.,  
 RA Yezaki Y., Takenawa T., Kadowaki T.;  
 RT "Insulin stimulates association of insulin receptor substrate-1 with  
 RT the protein abundant Src homology/growth factor receptor-bound  
 RT protein 2.";  
 RL J. Biol. Chem. 268:11167-11171(1993).  
 RN [7]  
 RP ASSOCIATION WITH IRS-1 AND SHC.  
 RX MEDLINE-93259135; PubMed-8491186;  
 RA Scolnik E.Y., Lee C.-H., Batzer A., Vincentini L.M., Zhou M., Daly R.,  
 RA Myers M.J., Jr., Backer J.M., Ullrich A., White M.F., Schlessinger J.;  
 RT "The SH2/SH3 domain-containing protein GRB2 interacts with tyrosine-  
 RT phosphorylated IRS1 and Shc: implications for insulin control of ras  
 RT signaling.";  
 RL EMBO J. 12:1929-1936(1993).  
 RN [8]  
 RP STRUCTURE BY NMR OF 1-56.  
 RX MEDLINE-97280795; PubMed-9135122;  
 RA Wittekind M., Mepelli C., Lee V., Goldfarb V., Friedrichs M.S.,  
 RA Meyers C.A., Mueller L.;  
 RT "Solution structure of the Grb2 N-terminal SH3 domain complexed with  
 RT a ten-residue peptide derived from SOS: direct refinement against  
 RT NOEs, J-couplings and 1H and 13C chemical shifts.";  
 RL J. Mol. Biol. 267:933-952(1997).  
 RN [9]  
 RP STRUCTURE BY NMR OF 60-158.  
 RX MEDLINE-96387228; PubMed-874768;  
 RA Thornton K.H., Mueller W.T., McConnell P., Zhu G., Saltiel A.R.,  
 RA Thanabal V.;  
 RT "Nuclear magnetic resonance solution structure of the growth factor  
 RT receptor-bound protein 2 Src homology 2 domain.";  
 RL Biochemistry 35:11852-11864(1996).  
 RN [10]  
 RP STRUCTURE BY NMR OF 53-163.  
 RX Senior M.M., Frederick A.F., Black S., Perkins L.M., Wilson O.,  
 RA Snow M.E., Wang Y.-S.;  
 RL Submitted (JUN-1997) to the PDB data bank.  
 RN [11]  
 RP STRUCTURE BY NMR OF 159-215.  
 RX MEDLINE-95187706; PubMed-7881903;  
 RA Konda D., Terasawa H., Ichikawa S., Ogura K., Hatanaka H.,  
 RA Mandiyan V., Ullrich A., Schlessinger J., Inagaki F.;

RT "Solution structure and ligand-binding site of the carboxy-terminal  
 RT SH3 domain of GRB2.";  
 RL Structure 2:1029-1040(1994).  
 RN [12]  
 RP X-RAY CRYSTALLOGRAPHY (3.1 ANGSTROMS).  
 RX MEDLINE-95232505; PubMed-7716522;  
 RA Maignan S., Guilloteau J.P., Fromage N., Arnoux B., Bequaert J.,  
 RA Ducruix A.;  
 RT "Crystal structure of the mammalian Grb2 adaptor.";  
 RL Science 268:291-295(1995).  
 RN [13]  
 RP X-RAY CRYSTALLOGRAPHY (1.8 ANGSTROMS) OF 56-153.  
 RX MEDLINE-98308003; PubMed-9642078;  
 RA Rahnel J., Garcia-Echeverria C., Furet P., Strauss A., Caravatti G.,  
 RA Fretz H., Schoepfer J., Gay B.;  
 RT "Structural basis for the high affinity of amino-aromatic SH2  
 RT phosphopeptide ligands.";  
 RL J. Mol. Biol. 279:1013-1022(1998).  
 RN [14]  
 RP X-RAY CRYSTALLOGRAPHY (2.1 ANGSTROMS) OF 49-163.  
 RX MEDLINE-99192587; PubMed-10090780;  
 RA Elmayer P., France D., Gounarides J., Jarosinski M., Martin M.-S.,  
 RA Rondeau J.-M., Sabio M., Topiol S., Weidmann B., Zurini M., Bair K.W.;  
 RT "Structural and conformational requirements for high-affinity binding  
 RT to the SH2 domain of Grb2(1).";  
 RL J. Med. Chem. 42:971-980(1999).  
 CC -1- FUNCTION: ASSOCIATES WITH ACTIVATED TYROSINE-PHOSPHORYLATED EGF  
 CC RECEPTORS AND PDGF RECEPTORS VIA ITS SH2 DOMAIN. GRB2 ALSO  
 CC ASSOCIATES TO OTHER CELLULAR TYROSINE-PHOSPHORYLATED PROTEINS SUCH  
 CC AS IRS-1, SHC AND LNK; PROBABLY VIA THE CONCERTED ACTION OF BOTH  
 CC ITS SH2 AND SH3 DOMAINS. IT ALSO SEEMS TO INTERACT WITH RAS  
 CC IN THE SIGNALING PATHWAY LEADING TO DNA SYNTHESIS. BINDS TO AND  
 CC TRANSLOCATES THE GUANINE NUCLEOTIDE EXCHANGE FACTORS SOS.  
 CC -1- FUNCTION: PROBABLY REPRESENTS A REGULATORY SUBUNIT OF DOWNSTREAM  
 CC SIGNALING MOLECULES WHOSE ACTIVITY IS MODULATED BY RECEPTOR  
 CC BINDING. A 55 KDA PHOSPHOPROTEIN OF UNKNOWN FUNCTION WHICH BINDS  
 CC TO GRB2 IN RESPONSE TO GROWTH FACTOR STIMULATION COULD BE A  
 CC DOWNSTREAM SIGNALING MOLECULE CANDIDATE.  
 CC -1- FUNCTION: ISOFORM GRB3-3 DOES NOT BIND TO PHOSPHORYLATED EPIDERMAL  
 CC GROWTH FACTOR RECEPTOR (EGFR) BUT INHIBITS EGF-INDUCED  
 CC TRANSACTIVATION OF A RAS-RESPONSIVE ELEMENT. GRB3-3 ACTS AS A  
 CC DOMINANT NEGATIVE PROTEIN OVER GRB2 AND BY SUPPRESSING  
 CC PROLIFERATIVE SIGNALS, MAY TRIGGER ACTIVE PROGRAMMED CELL DEATH.  
 CC -1- ALTERNATIVE PRODUCTS: A NUMBER OF FORMS ARE PRODUCED BY  
 CC ALTERNATIVE SPLICING.  
 CC -1- TISSUE SPECIFICITY: WIDE TISSUE AND CELL DISTRIBUTION.  
 CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.  
 CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.  
 CC -1- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.  
 CC -----  
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 CC -----  
 DR EMBL: M96995; AAA58448.1; -  
 DR EMBL: X62852; CAA44664.1; -  
 DR EMBL: X62853; CAA44665.1; -  
 DR EMBL: D49846; BAA08645.1; -  
 DR EMBL: L29511; AAC37549.1; -  
 DR EMBL: AF063618; AAC72075.1; -  
 DR EMBL: AF063614; AAC72075.1; JOINED.  
 DR EMBL: AF063615; AAC72075.1; JOINED.  
 DR EMBL: AF063616; AAC72075.1; JOINED.  
 DR EMBL: AF063617; AAC72075.1; JOINED.  
 DR PIR: AA3321; A43321.  
 DR PIR: S26050; S26050.  
 DR PDB: 1GRI; 08-MAR-96.  
 DR PDB: 1GRC; 31-AUG-94.  
 DR PDB: 1GRD; 31-AUG-94.

DR PDB; 1GHU; 27-JAN-97.  
 DR PDB; 1TZE; 07-JUL-97.  
 DR PDB; 1FHS; 17-JUN-98.  
 DR PDB; 1BM2; 05-AUG-98.  
 DR PDB; 1BMB; 29-JUL-98.  
 DR PDB; 1ZEP; 30-MAR-99.  
 DR MIM; 108355; -.  
 DR InterPro; IPR000980; -.  
 DR InterPro; IPR01452; -.  
 DR Pfam; PF00017; SH2; 1.  
 DR Pfam; PF00018; SH3; 2.  
 DR PRINTS; PR00401; SH2DOMAIN.  
 DR PRINTS; PR00452; SH3DOMAIN.  
 DR PROSITE; PS50001; SH2; 1.  
 DR PROSITE; PS50002; SH3; 2.  
 DR SH2 domain; SH3 domain; Alternative splicing; 3D-structure.  
 FT DOMAIN 1 58 SH3.  
 FT DOMAIN 60 152 SH2.  
 FT DOMAIN 156 215 SH3.  
 FT VARSPPLIC 60 100 MISSING (IN ISOFORM GRB3-3).  
 FT VARSPPLIC 157 170 MISSING (IN ISOFORM ASH-M).  
 FT MUTAGEN 49 49 P->L: INEFFECTIVE IN DNA SYNTHESIS.  
 FT MUTAGEN 203 203 G->R: INEFFECTIVE IN DNA SYNTHESIS.  
 SO SEQUENCE 217 AA; 25206 MW; 83A4B0BA1B248DC4 CRC64;

Query Match 13.2%; Score 224; DB 1; Length 217;  
 Best Local Similarity 27.9%; Pred. No. 1.5e-09;  
 Matches 53; Conservative 44; Mismatches 57; Indels 36; Gaps 7;

QY 7 NFDSESSSWYGRSLRQDAVALLOGRH-GVFLYRDSSTSGDYLVSYSENSRVSHYII 65  
 DB 51 NTEKMPHFMPFGKIPRAKAEMLERKRDHGAFLIRESEASAPDESLSKVFENDVQHFYV 110  
 QY 66 NSSGPRPVPPADPPVSPSRLRIGQEDPSLPALLEFKIHYLDTTTLEPVARSR 125  
 DB 111 LNDG-----AGKIFLWYVKNLSNLEVDYHR-----STS---VSRNQ 144  
 QY 126 QSGSVILRQ----EEAYRALPFGNDEBDLPFKKGDILIRDKPEEQWMAEDSEG 180  
 DB 145 Q---IFLRDIEGVPOQPTVYQALPFDPEDEGLFRRDQFLHVMNDSPPNMWKA-CHG 200  
 QY 181 KRGKTPVPYV 190  
 DB 201 QRGMEPRNTV 210

RESULT 13  
 GRB2\_MOUSE STANDARD; PRT; 217 AA.  
 AC Q60631; Q61240;  
 DT 01-NOV-1997 (Rel. 35, Created)  
 DT 01-NOV-1997 (Rel. 35, Last sequence update)  
 DT 15-JUL-1999 (Rel. 38, Last annotation update)  
 DE GROWTH FACTOR RECEPTOR-BOUND PROTEIN 2 (GRB2 ADAPTER PROTEIN)  
 DE (SH2/SH3 ADAPTER GRB2).  
 GN GRB2.  
 OS Mus musculus (Mouse).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.  
 OX NCBI\_Taxid=10090;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC STRAIN-BALB/C;  
 RC MEDLINE=93360985; Pubmed=7689150;  
 RA Suen K., Bustelo X.R., Pawson T., Barbacid M.:  
 RT "Molecular cloning of the mouse grb2 gene: differential interaction  
 RT of the Grb2 adaptor protein with epidermal growth factor and nerve  
 RT growth factor receptors.";  
 RL Mol. Cell. Biol. 13:5500-5512(1993).  
 RN [2]  
 RP SEQUENCE FROM N.A. (ISOFORM GRB3-3).  
 RC STRAIN-BALB/C;

RA Tanaka S.;  
 RN Submitted (JUN-1996) to the EMBL/GenBank/DBJ databases.  
 RL [3]  
 RP STRUCTURE BY NMR OF 1-59.  
 RX MEDLINE=97280795; Pubmed=9135122;  
 RA Wittekind M., Kapell C., Lee V., Goldfarb V., Friedrichs M.S.,  
 RA Meyers C.A., Mueller L.;  
 RT "Solution structure of the Grb2 N-terminal SH3 domain complexed with  
 RT a ten-residue peptide derived from SOS: direct refinement against  
 RT NOES, J-couplings and 1H and 13C chemical shifts.";  
 RL J. Mol. Biol. 267:933-952(1997).  
 CC -I- FUNCTION: ASSOCIATES WITH ACTIVATED TYROSINE-PHOSPHORYLATED EGF  
 CC RECEPTORS AND PDGF RECEPTORS VIA ITS SH2 DOMAIN. GRB2 ALSO  
 CC ASSOCIATES TO OTHER CELLULAR TYROSINE-PHOSPHORYLATED PROTEINS SUCH  
 CC AS IRS-1, SHC AND LNK. PROBABLY VIA THE CONCERTED ACTION OF BOTH  
 CC ITS SH2 AND SH3 DOMAINS. IT ALSO SEEMS TO INTERACT WITH RAS  
 CC IN THE SIGNALING PATHWAY LEADING TO DNA SYNTHESIS. BINDS TO AND  
 CC TRANSLOCATES THE GUANINE NUCLEOTIDE EXCHANGE FACTORS SOS.  
 CC -I- FUNCTION: PROBABLY REPRESENTS A REGULATORY SUBUNIT OF DOWNSTREAM  
 CC SIGNALING MOLECULES WHOSE ACTIVITY IS MODULATED BY RECEPTOR  
 CC BINDING. A 55 KDA PHOSPHOPROTEIN OF UNKNOWN FUNCTION WHICH BINDS  
 CC TO GRB2 IN RESPONSE TO GROWTH FACTOR STIMULATION COULD BE A  
 CC DOWNSTREAM SIGNALING MOLECULE CANDIDATE.  
 CC -I- FUNCTION: ISOFORM GRB3-3 DOES NOT BIND TO PHOSPHORYLATED EPIDERMAL  
 CC GROWTH FACTOR RECEPTOR (EGFR) BUT INHIBITS EGF-INDUCED  
 CC TRANSACTIVATION OF A RAS-RESPONSIVE ELEMENT. GRB3-3 ACTS AS A  
 CC DOMINANT NEGATIVE PROTEIN OVER GRB2 AND BY SUPPRESSING  
 CC PROLIFERATIVE SIGNALS, MAY TRIGGER ACTIVE PROGRAMMED CELL DEATH  
 CC (BY SIMILARITY).  
 CC -I- ALTERNATIVE PRODUCTS: A NUMBER OF FORMS ARE PRODUCED BY  
 CC ALTERNATIVE SPLICING.  
 CC -I- SIMILARITY: CONTAINS 1 SH2 DOMAIN.  
 CC -I- SIMILARITY: CONTAINS 2 SH3 DOMAINS.  
 CC -I- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.  
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 CC -----  
 CC EMBL; U07617; AAB40022.1; -.  
 CC EMBL; D85748; BAA12862.1; -.  
 DR PDB; 1GBQ; 04-SEP-97.  
 DR PDB; 2GBQ; 04-SEP-97.  
 DR PDB; 3GBQ; 04-SEP-97.  
 DR PDB; 4GBQ; 04-SEP-97.  
 DR PDB; 1GBR; 26-JAN-95.  
 DR MGD; MGI:95805; Grb2.  
 DR InterPro; IPR000980; -.  
 DR InterPro; IPR001452; -.  
 DR Pfam; PF00017; SH2; 1.  
 DR Pfam; PF00018; SH3; 2.  
 DR PRINTS; PR00401; SH2DOMAIN.  
 DR PRINTS; PR00452; SH3DOMAIN.  
 DR PROSITE; PS50001; SH2; 1.  
 DR PROSITE; PS50002; SH3; 2.  
 KW SH2 domain; SH3 domain; Alternative splicing; 3D-structure.  
 FT DOMAIN 1 58 SH3.  
 FT DOMAIN 60 152 SH2.  
 FT VARSPPLIC 60 100 MISSING (IN ISOFORM GRB3-3).  
 SO SEQUENCE 217 AA; 25238 MW; 97FAA4FB4B248DDF CRC64;

QY 7 NFDSESSSWYGRSLRQDAVALLOGRH-GVFLYRDSSTSGDYLVSYSENSRVSHYII 65  
 DB 51 NTEKMPHFMPFGKIPRAKAEMLERKRDHGAFLIRESEASAPDESLSKVFENDVQHFYV 110  
 QY 66 NSSGPRPVPPADPPVSPSRLRIGQEDPSLPALLEFKIHYLDTTTLEPVARSR 125  
 DB 111 LNDG-----AGKIFLWYVKNLSNLEVDYHR-----STS---VSRNQ 144  
 QY 126 QSGSVILRQ----EEAYRALPFGNDEBDLPFKKGDILIRDKPEEQWMAEDSEG 180  
 DB 145 Q---IFLRDIEGVPOQPTVYQALPFDPEDEGLFRRDQFLHVMNDSPPNMWKA-CHG 200  
 QY 181 KRGKTPVPYV 190  
 DB 201 QRGMEPRNTV 210

Query Match 13.2%; Score 224; DB 1; Length 217;  
 Best Local Similarity 27.9%; Pred. No. 1.5e-09;  
 Matches 53; Conservative 44; Mismatches 57; Indels 36; Gaps 7;

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Db 51 NYIEMKPHWPFEGKIPRAKAEMLSKQRHDAFLIRESESAPGDSLSVKFGNDVQHFXY 110
QY 66 NSSGPRPVPPSPAPPPGVSPSRRLIGDOFDSLPALEFYKIHVDTTLLIEPVARSR 125
Db 111 LRDS-----AGKYILWVVKFNSLNELVDYHR-----STS-----YSRNO 144
QY 126 QGSGVILRO-----EEAEYRALFPNGNDEEDLPFKKGDIILIRDKPEEOMNAEDSEG 180
Db 145 Q---IFLRDIEQVPOOPTYVQALFDPQEGELGFRGRDGFIVHMDSNDPMWKGK-CHG 200
QY 181 KRGMIPVPYV 190
Db 201 QTGMFPRNTV 210

RESULT 14
GRB2.CHICK STANDARD; PRT; 217 AA.
AC Q07883;
DT 01-FEB-1995 (Rel. 31, Created)
DT 01-FEB-1995 (Rel. 31, Last sequence update)
DT 15-JUL-1999 (Rel. 38, Last annotation update)
DE GROWTH FACTOR RECEPTOR-BOUND PROTEIN 2 (GRB2 ADAPTER PROTEIN)
DE (SH2/SH3 ADAPTER GRB2) (ASH PROTEIN).
GN GRB2.
OS Gallus gallus (Chicken).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Archosauria; Aves; Neognathae; Galliformes; Phasianidae; Phasianinae;
OC Gallus.
OC NCBI_TaxID=9031;
RN [1]
RP SEQUENCE FROM N.A.
RC TISSUE-Brain:
RX MEDLINE=94085795; PubMed=8262390;
RT "Sequence of a chicken cDNA encoding a GRB2 protein.";
RL Gene 134:299-300(1993).
CC -1- FUNCTION: ASSOCIATES WITH ACTIVATED TYROSINE-PHOSPHORYLATED EGF
CC RECEPTORS AND PDGF RECEPTORS VIA ITS SH2 DOMAIN. GRB2 ALSO
CC ASSOCIATES TO OTHER CELLULAR TYROSINE-PHOSPHORYLATED PROTEINS SUCH
CC AS IRS-1, SHC AND LNK. PROBABLY VIA THE CONCERTED ACTION OF BOTH
CC ITS SH2 AND SH3 DOMAINS. IT ALSO SEEMS TO INTERACT WITH RAS
CC IN THE SIGNALING PATHWAY LEADING TO DNA SYNTHESIS. BINDS TO AND
CC TRANSLOCATES THE GUANINE NUCLEOTIDE EXCHANGE FACTORS SOS.
CC -1- FUNCTION: PROBABLY REPRESENTS A REGULATORY SUBUNIT OF DOWNSTREAM
CC SIGNALING MOLECULES WHOSE ACTIVITY IS MODULATED BY RECEPTOR
CC BINDING. A 55 KDA PHOSPHOPROTEIN OF UNKNOWN FUNCTION WHICH BINDS
CC TO GRB2 IN RESPONSE TO GROWTH FACTOR STIMULATION COULD BE A
CC DOWNSTREAM SIGNALING MOLECULE CANDIDATE.
CC -1- TISSUE SPECIFICITY: WIDE TISSUE AND CELL DISTRIBUTION.
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
CC -1- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.
CC -----
CC This SWISS-PROT entry is copyright. It is produced through a collaboration
CC between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC the European Bioinformatics Institute. There are no restrictions on its
CC use by non-profit institutions as long as its content is in no way
CC modified and this statement is not removed. Usage by and for commercial
CC entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC or send an email to license@isb-sib.ch).
CC -----
CC EMBL: L19258; AAA16318.1; -.
CC PIR: J70664; J70664.
CC HSSP: P29354; 1GRI.
CC InterPro: IPR000980; -.
CC InterPro: IPR001452; -.
CC Pfam: PF00017; SH2; 1.
CC Pfam: PF00018; SH3; 2.
CC PRINTS: PR00452; SH3DOMAIN.
CC PROSITE: PS50001; SH2; 1.
CC PROSITE: PS50002; SH3; 2.
CC SH2 domain; SH3 domain.
KW

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FT DOMAIN 1 58 SH3.
FT DOMAIN 60 152 SH2.
FT DOMAIN 156 215 SH3.
SQ SEQUENCE 217 AA; 25076 MW; DDC9A84ECD52859 CRC64;

Query Match 12.9%; Score 218; DB 1; Length 217;
Best Local Similarity 27.9%; Pred. No. 4,1e-09;
Matches 53; Conservative 44; Mismatches 57; Indels 36; Gaps 7;

QY 7 NFDSEERSWYWGRLSROAVALLQGRH-GVEIYRSDSTSPGIVLSVSENSRSHYII 65
Db 51 NYIEMKPHWPFEGKIPRAKAEMLSKQRHDAFLIRESESAPGDSLSVKFGNDVQHFXY 110
QY 66 NSSGPRPVPPSPAPPPGVSPSRRLIGDOFDSLPALEFYKIHVDTTLLIEPVARSR 125
Db 111 LRDS-----AGKYILWVVKFNSLNELVDYHR-----STS-----YSRNO 144
QY 126 QGSGVILRO-----EEAEYRALFPNGNDEEDLPFKKGDIILIRDKPEEOMNAEDSEG 180
Db 145 Q---IFLRDIEQVPOOPTYVQALFDPQEGELGFRGRDGFIVHMDSNDPMWKGK-CHG 200
QY 181 KRGMIPVPYV 190
Db 201 QTGMFPRNTV 210

RESULT 15
GRB2.XENLA STANDARD; PRT; 217 AA.
AC P87379;
DT 15-DEC-1998 (Rel. 37, Created)
DT 15-DEC-1998 (Rel. 37, Last sequence update)
DT 15-JUL-1999 (Rel. 38, Last annotation update)
DE GROWTH FACTOR RECEPTOR-BOUND PROTEIN 2 (GRB2 ADAPTER PROTEIN)
DE (SH2/SH3 ADAPTER GRB2).
GN GRB2.
OS Xenopus laevis (African clawed frog).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Amphibia; Batrachia; Anura; Mesobatrachia; Pipidae;
OC Xenopodinae; Xenopus.
OC NCBI_TaxID=6355;
RN [1]
RP SEQUENCE FROM N.A.
RL "La W., Mayer B.J.;
RX Submitted (FEB-1997) to the EMBL/Genbank/DBJ databases.
CC -1- FUNCTION: ASSOCIATES WITH ACTIVATED TYROSINE-PHOSPHORYLATED EGF
CC RECEPTORS AND PDGF RECEPTORS VIA ITS SH2 DOMAIN. GRB2 ALSO
CC ASSOCIATES TO OTHER CELLULAR TYROSINE-PHOSPHORYLATED PROTEINS SUCH
CC AS IRS-1, SHC AND LNK. PROBABLY VIA THE CONCERTED ACTION OF BOTH
CC ITS SH2 AND SH3 DOMAINS. IT ALSO SEEMS TO INTERACT WITH RAS
CC PROTEINS IN THE SIGNALING PATHWAY LEADING TO DNA SYNTHESIS (BY
CC SIMILARITY).
CC -1- FUNCTION: PROBABLY REPRESENTS A REGULATORY SUBUNIT OF DOWNSTREAM
CC SIGNALING MOLECULES WHOSE ACTIVITY IS MODULATED BY RECEPTOR
CC BINDING. A 55 KDA PHOSPHOPROTEIN OF UNKNOWN FUNCTION WHICH BINDS
CC TO GRB2 IN RESPONSE TO GROWTH FACTOR STIMULATION COULD BE A
CC DOWNSTREAM SIGNALING MOLECULE CANDIDATE (BY SIMILARITY).
CC -1- SIMILARITY: CONTAINS 1 SH2 DOMAIN.
CC -1- SIMILARITY: CONTAINS 2 SH3 DOMAINS.
CC -1- SIMILARITY: BELONGS TO THE GRB2 / SEM-5 / DRK FAMILY.
CC -----
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CC or send an email to license@isb-sib.ch).
CC -----
CC EMBL: U89775; AAA49699.1; -.
CC InterPro: IPR000980; -.
CC InterPro: IPR001452; -.

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